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AU 1638

THE UNITED STATES PATENT AND TRADEMARK OFFICE
Re: Appeal to the Board of Appeals

In re Application of	)	
	)	
AMMERMANN et al.	)	Group Art Unit: 1638
	)	
Serial No. 09/403,654	)	Examiner: D. Kruse
	)	
Filed: October 25, 1999	)	
	)	

For: EXPRESSION OF FUNGICIDE-BINDING POLYPEPTIDES IN PLANTS FOR GENERATING FUNGICIDE TOLERANCE

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on:
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Jason D. Voight
Person Making Deposit
Jason D. Voight
Signature
May 3, 2002
Date of Signature

1. [ ] NOTICE OF APPEAL: Applicant hereby appeals to the Board of Appeals from the decision dated _____ of the Primary Examiner finally rejecting claims ____.
2. [X] A check to cover the extension fee of $ 720.00 is enclosed.
3. [X] BRIEF on appeal in this application is transmitted herewith.
4. [ ] An Oral Hearing is requested.
   [ ] The Oral Hearing fee of $280.00 is enclosed.
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6. [X] The Commissioner is hereby authorized to charge any fees which may be further required, or credit any over payment to Account No. 11-0345. A duplicate copy of this sheet is attached.

Respectfully submitted,
KEIL & WEINKAUF

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#16

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of	)	
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AMMERMANN et al.	)	Group Art Unit: 1638
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For: EXPRESSION OF FUNGICIDE-BINDING POLYPEPTIDES IN PLANTS FOR GENERATING FUNGICIDE TOLERANCE

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

BRIEF ON APPEAL

This appeal is from the examiner's Final Rejection of July 17, 2001.

REAL PARTY IN INTEREST

The real party in interest is BASF Aktiengesellschaft of Ludwigshafen, Germany.

RELATED APPEALS AND INTERFERENCES

To the best of the undersigned's knowledge, there are no related appeals or interferences within the meaning of 37 CFR 1.192(c).

STATUS OF CLAIMS

Claims 29-36, 39, 41-46 and 49-51 are before the Board. A copy of these claims is appended hereto.

STATUS OF AMENDMENTS

Appellants filed amendments under 37 CFR 1.116 on October 18, 2001 and March 6, 2002, the latter of which included the enclosed declaration. These papers were entered.

SUMMARY OF INVENTION

As set out in the claims, the instant invention relates to a process for the production of plants having improved fungicide/herbicide tolerance by transforming the plants with a gene encoding for a polypeptide which binds the fungicide/herbicide. In claims 29-36, 39, 46 and 51 said gene is limited to one produced and isolated by

a) immunizing an animal with methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F) to produce a polyclonal serum of said polypeptide,

b) producing a monoclonal cell line to produce a specific, monoclonal methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide,

c) isolating the mRNA encoding said monoclonal polypeptide of step b) from said monoclonal cells and synthesizing the corresponding cDNA encoding said polypeptide.

ISSUES

Whether claims 29-36, 39, 41-46 and 49-51 have been properly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Whether claims 29-36, 39, 41-46 and 49-51 have been properly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

GROUPING OF CLAIMS

Claims 29-31 are directed to a process for the production of a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-tolerant plant. Claims 32-36 and 51 are directed to an expression cassette. Claim 39 is directed to a selection marker. Claims 41-44 and 49-50 are directed to a process for the transformation of a plant or cells of a plant. Claim 45 is directed to a process for production of a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide. Claim 46 is directed to a plant.

All of the claims relate to a gene encoding a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide. In claims 29-36, 39, 46 and 51 said gene is limited to one produced and isolated by steps expressly stated therein. Therefore, claims 29-36, 39, 46 and 51 do not stand or fall together with claims 41-45 and 49-50. Further, claims 29-31 are directed to a process, rather than a product, expressly containing limitations directed to the production and isolation of the gene. Therefore, claims 29-31 do not stand or fall together with claims 32-36, 39, 41-46 and 49-51.

ARGUMENT

Appellants submit that the instant invention is described and enabled by the instant specification as filed.

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 514 F.2d

257, 263, 191 USPQ 90, 97 (CCPA 1976) ("the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims").

First, it should be emphasized that the instant invention provides a completely novel way for producing herbicide/fungicide-resistant or -tolerant plants. The advantage is that, in contrast to previously known methods, no detailed knowledge of either the molecular mechanism of herbicidal action in the plant or of plant enzymes and their encoding genes of essential biosynthetic pathways involved in imparting herbicide resistance is required. The emphasis in the present invention lies upon the expression of an "exogenous" polypeptide, antibody, or part of an antibody. Thereby "exogenous" in the sense of the present invention means, that the antibody does *not* act via any kind of *endogenous* component, like an enzyme or gene of an essential biosynthetic pathway or via endogenous components involved in gene expression or enzyme activity or other endogenous metabolites of a plant or microorganism, but solely via a *non-endogenous*, i.e. via an exogenous antigen, here preferably the chemically synthesized herbicide. This is a great advantage of the instant invention, because no detailed knowledge about endogenous mechanisms, genes, enzymes etc. are necessary. The present invention is absolutely independent from this biochemical or genetic information. Only the availability of the herbicide as a chemical compound itself is sufficient to produce a herbicide-tolerant or -resistant transgenic plant. The disclosure of this context is given on page 4, line 33 to page 5, line 11 of the instant specification.

Further, the method for producing the specific antibody against an exogenous antigen and the steps how to clone the relevant gene coding for this exogenous antibody are disclosed in detail in the specification at page 5, line 17 ff. Here the herbicide is used to immunize a vertebrate which itself produces an antibody against this herbicide. The antiserum is isolated from the immunized vertebrate and used to produce a specific monoclonal antibody following art known techniques of hybridoma cell cultures. The mRNA encoding the herbicide specific monoclonal antibody is isolated from the hybridoma cells and subsequently the cDNA encoding the monoclonal antibody or a part of the monoclonal antibody is prepared, e.g. via PCR. Then the cDNA is cloned into an expression cassette or a phage display library to test the functional expression in prokaryotic or eukaryotic organisms, e.g. in plants. After transformation of the of the cDNA (in a suitable expression cassette) into the plant, a polypeptide with specific antigenic function is expressed which binds to the fungicide molecules applied to the plant and converts the fungicide into a complex which has non-fungicidal properties. Thus, the instant application provides a person skilled in the art with the exact information for producing a fungicide-resistant or -tolerant plant.

Another advantage of the instant invention is, that during PCR with the isolated cDNA prepared from the monoclonal antibody producing hybridoma cells described above, only the variable single chain fragments (scFv) of the antibody can be amplified (as discussed further below).

The primers suitable for amplification of the scFv of an antibody via PCR are known to one skilled in the art, since every nucleotide sequence encoding a variable

single chain fragment of an antibody contains, in addition to the specific antigen determinate, some conserved regions. Therefore, it should not be necessary to state the primer sequences explicitly.

The advantages of the variable single chain fragment (scFv) of an antibody of the present invention over a whole antibody are as follows: the scFv is the reaction specific part of the antibody involved in the antigen-antibody-interaction and what was shown in the present invention is that the present scFv is sufficient to "inactivate" the herbicide through binding the herbicide and converting it into a non-functional complex; the present scFv is easier to handle than the whole antibody, e.g. concerning the expression and assembly in the plant cell(the whole antibody with its light and heavy chains would not assemble in the plant cytoplasm); further it is not necessary to construct and breed two different plant cell lines in time consuming procedures each encoding for the light and heavy chains of an antibody , respectively. Moreover, the expression of scFv in the plant cell and the scFv itself is more stable than the complete antibody. Therefore, the plants encoding the present herbicide-specific scFv also show specific tolerance or resistance against a special kind of herbicide and are more stable than plants expressing the whole antibody. Finally, the plant specificity against a defined herbicide is of immense importance for agricultural use of plants provided by the instant invention.

In summary, the present application discloses a novel route and working guide for the general production of any kind of herbicide-tolerant or -resistant plants without

the knowledge of biochemical or genetic mechanisms of action of the herbicide. Through the novel method of expressing an *exogenous* antibody or part thereof in plants, the present invention delivers a quick and advantageous *method* for producing specific herbicide-tolerant or -resistant plants. No such method was known at the time of the present invention. The scFv encoding nucleotide sequence itself and its disclosure is of minor importance to the underlying novel and inventive method.

The Examiner demands description of "a DNA sequence as claimed" (Office action of November 2, 2001). Appellants note that claims 29-31, in particular, are not directed to "a DNA sequence," but rather to a process for producing a herbicide/fungicide-tolerant plant. To the extent the Office finds that these or other claims contain product-by-process elements, appellants note that "[w]here the process has actually been used to produce the product, the written description requirement for a product-by-process claim is clearly satisfied." MPEP 2163. As discussed above, knowledge of a DNA sequence is not necessary to practice the invention, but rather the invention is practiced by carrying out the process steps set out in the claims. The enclosed declaration further demonstrates that one of ordinary skill in the art would have recognized that applicants had possession of the claimed invention.

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the [application] coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). "Enablement is not precluded by the necessity for some experimentation such as routine screening." *In re*

Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The examiner should always look for enabled, allowable subject matter and communicate to application what that subject matter is at the earliest possible point in the prosecution. MPEP 2164.04.

The Examiner concludes that one of skill in the art would not be able to reisolate a specific nucleotide encoding sequence of the claimed plant. Applicants again note that claims 29-31, in particular, are not directed to a DNA sequence, but rather to a process for producing a herbicide/fungicide-tolerant plant. The process does not require knowledge of a DNA sequence, but rather the specification provides guidance as to how to obtain such a sequence and use it to transform a plant. The focus of the present invention is the unconventional method of isolating from an animal gene a sequence encoding an antibody which acts against herbicides/fungicides in plants. Concrete steps of this novel method of producing herbicide/fungicide resistant plants are disclosed in detail in the specification. Identification and isolation of genes encoding *all* peptides that bind the herbicide/fungicide is *not* necessary to practice the present invention. The Examiner gives no explanation supporting a conclusion that one reasonably skilled in the art could not make or use said process without undue experimentation. As evidenced by the enclosed declaration, one of ordinary skill in the art would have understood the process steps involved and been able to make and use the invention.

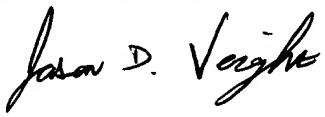
Therefore, reversal of the Examiner's rejection is solicited.

Please find attached a check for $720.00 for filing fee and two month extension of time fee.

Please charge any other shortage in fees due in connection with the filing of this paper to Deposit Account No. 11-0345. Please credit any excess fees to such deposit account.

Respectfully submitted,

KEIL & WEINKAUF



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APPENDIX

29. A process for the production of a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-tolerant plant, said process comprising transforming a plant with a gene encoding a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide, whereby said polypeptide and the corresponding gene encoding said polypeptide is produced exogenously and isolated by the following steps:

a) immunizing an animal with methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F) to produce a polyclonal serum of said polypeptide,

b) producing a monoclonal cell line to produce a specific, monoclonal methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide,

c) isolating the mRNA encoding said monoclonal polypeptide of step b) from said monoclonal cells and synthesizing the corresponding cDNA encoding said polypeptide.

30. The process as claimed in claim 29, wherein the methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide is a single-chain antibody fragment.

31. The process as claimed in claim 29, wherein the methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide is a complete antibody or a binding fragment of a complete antibody.

32. An expression cassette for plants, comprising a promoter, a nucleotide sequence encoding a signal peptide, a gene encoding an exogenous methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide or a part thereof produced according to steps a)-c) of claim 29, and a nucleotide sequence encoding an ER retention signal and a terminator.

33. The expression cassette as claimed in claim 32, wherein the promoter is constitutive.

34. The expression cassette as claimed in claim 32, wherein the gene encodes a single-chain antibody fragment.

35. The expression cassette as claimed in claim 32, wherein the gene encodes a fusion protein comprising a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide or a part thereof and at least one other functional protein or a part thereof selected from the group consisting of enzymes, toxins, chromophores and binding proteins.

36. The expression cassette as claimed in claim 32, wherein the gene is isolated from a hybridoma cell or with the aid of other recombinant methods.

39. A selection marker comprising the expression cassette as claimed in claim 32.

41. A process for the transformation of a plant or cells of a plant, said process comprising introducing a gene sequence which encodes a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide into the

plant or the cells of the plant.

42. The process as claimed in claim 41, wherein the introducing is effected by an *Agrobacterium*.

43. The process as claimed in claim 41, wherein the introducing is effected by electroporation.

44. The process as claimed in claim 41, wherein the introducing is effected by the particle bombardment method.

45. A process for production of a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide, said process comprising transforming a plant or cells of a plant with a gene which encodes such a polypeptide and subsequently isolating the polypeptide.

46. A plant comprising the expression cassette as claimed in claim 33, wherein the expression cassette imparts increased tolerance to the plant, relative to a wild type or non-transformed plant, against methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F).

49. The process as claimed in claim 41, wherein the gene sequence which encodes a methyl methoxyimino-α-(o-tolyloxy)-o-tolylacetate (BAS 490F)-binding polypeptide is part of an expression cassette which also comprises a signal peptide, an ER retention signal and a terminator.

50. The process as claimed in claim 42, wherein the *Agrobacterium* is of the species *Agrobacterium tumefaciens*.

51. The expression cassette as claimed in claim 33, wherein the constitutive promoter is the CaMV 35S promoter.